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(54) Title: TOPICAL COMPOSITIONS

(57) Abstract

Topical compositions of urea, useful for the prevention and/or reduction of skin damage caused by ultraviolet radiation.

TOPICAL COMPOSITIONS

This invention relates to topical c mpositions for the prevention and/or reduction of skin damage caused by ultraviolet radiation. In particular this invention relates to the prevention and/or reduction of skin damage caused by reactive chemical substances generated in the skin by ultraviolet radiation.

The health promoting qualities of sunlight have been recognized throughout history. However, in recent years, medical professionals and the lay public both have become awre of the skin diseases and degenerative processes that occur from prolonged and excessive exposure to ultraviolet (UV) radiation. Depending on skin types, even modest exposure can be damaging and dangerous.

The mechanisms by which ultraviolet radiation exerts its adverse effects on the skin are not fully understood. They are believed to involve absorption of light energy by skin tissue components to produce very reactive substances such as free radicals. In particular, they involve the production in the skin tissue of nitroso, nitrite, and other mediators of undesired skin changes in sensitive individuals. The potential of nitrites to react with and damage tissue is well recognized. Recent experiments in vitro and in vivo have shown the contribution of nitrites to structual alteration of integumental (skin) structures.

Prior art topical compositions-for the prevention of UV induced skin damage-are essentially sunscreens in that they absorb light particularly in the ultraviolet wave lengths associated with skin damage. Even with the broad spectrum of sunscreen preparations available, ranging from modest to essentially complete UV blockage, serious problems of sun damaged skin persist. These sunscreens are not effective in reducing the formation of free radical substances such as nitrate reduction products in

the skin tissue from UV light that does reach the skin. Furthermore, they do not have any effect on the damaging interactions in the skin tissue caused by the free radicals produced.

The present invention provides a topical urea composition, for prevention of skin damage due to ultraviolet radiation.

Since urea has no ultraviolet light absorbing properties in the skin damaging light wave lengths of 290 to 400 mm, it is not a sunscreen agent. Its skin protective properties are as a neutralizer of damaging active chemical entities. Urea moderates the effects of nitrate reduction products, thus preventing skin damage following ultraviolet radiation.

The concentration of urea which may be used in the topical compositions is from about 0.1% to about 40%, preferably from about 1% to about 20% based on the weight of the composition.

It is a further embodiment of this invention to use chemical analogs of urea which have functional urea substitutions, in the topical compositons.

In a preferred embodiment of this invention urea may be combined with known UV absorbing sun screen agents such as Padimato O (2-ethylhexyl-p-dimethyl amino-benzoate), Oxybenzone (2-hydroxy-4-methoxy benzophenone) and paraaminobenzoic acid (PABA) in topical compositions. This combination of UV absorbing agents and urea free radical neutralizer, provides a superior skin protecting agent to that of the prior art.

The UV absorbing agent may be present in the topical composition from about 1% to about 10% by weight of the composition.

The topical compositions of this invention are preferably applied to the skin in the form of conventional alcoholic lotions, liquid emulsions, creams, transparent gels, or aerosol sprays.

EXAMPLE

The following ingredients were blended to form topical cream compositions (A, B, C, D and E) using conventional methods.

Ingredients	Percent w/w A	B	C	D	E
Mineral Oil	5-20	5-20	5-20	5-20	5-20
Isopropyl Myristate	0-10	0-10	0-10	0-10	0-10
Acetylated Lanolin Alcohol	0-10	0-10	0-10	0-10	0-10
Cetyl Alcohol	1-10	1-10	1-10	1-10	1-10
Glycerol Mono-stearate	1-10	1-10	1-10	1-10	1-10
Tween 80	0-5	0-5	0-5	0-5	0-5
Methyl Paraffin	0.5	0.5	0.5	0.5	0.5
Propyl Paraffin	0.2	0.2	0.2	0.2	0.2
Carbopol 934 (Polyacrylic acid)	0.1	0.1	0.1	0.1	0.1
Sodium Hydroxide	0-0.1	0-0.1	0-0.1	0-0.1	0-0.1
Propyleneglycol	0-5	0-5	0-5	0-5	0-5
Urea	15	-	15	-	15
X Padimate O (2-ethylhexyl-p-di-methyl amino-benzoate)	-	1.4-8	1.4-8	-	-
X Oxybenzone (2-Hydroxy-4-Methoxy Benzophenone)	-	-	-	2-6	2-6
Water	q.s.	q.s.	q.s.	q.s.	q.s.
Total	100	100	100	100	100

x = sunscreen.

In a study of ultraviolet light induced acute and chronic actinic damage, it was found that the urea compositions of this invention (e.g., compositions A, C and E) provided a significant degree of protection against acute sunburn damage in hairless mouse skin as compared with placebo compositions. Using SK-1 hairless mice, observations were made of erythema responses under blinded conditions. There were striking differences in H and E stained tissue sections taken from the reaction sites. The skin damage in placebo treated sites was two to three times greater than the urea composition treated sites, based upon thickness of the epidermis, the number of sunburn cells noted, and the dermal inflammatory changes.

WHAT IS CLAIMED IS:

1. A method for the prevention and/or reduction f skin damage caused by ultraviolet rdiation which comprises topically applying a composition of a therapeutically effective amount of urea in a pharmaceutically acceptable carrier to the skin of an individual in need of such skin treatment.

2. The method according to claim 1 wherein the amount of urea is from about 0.1 to about 40 percent based on the weight of the composition.

3. The method according to claim 2 wherein the amount of urea is from 1 to about 20 percent.

4. The method according to claim 1 wherein an ultraviolet radiation absorbing agent is present in the composition.

5. The method according to claim 4 wherein the ultraviolet radiation absorbing agent is 2-ethyl-hexyl-p-dimethyl aminobenzoate, 2-hydroxy-4-methoxy benzophenoue, or para-aminobenzoic acid.

6. The method according to claim 5 wherein the amount of ultraviolet absorbing agent is from about 1 to about 10 percent based on the weight of the composition.

7. A composition for the prevention and/or reduction of skin damage caused by ultraviolet radiation which comprises a therapeutically effective amount of urea and a therapeutically effective amount of an ultraviolet radiation absorbing agent.

8. The composition according to claim 7 wherein the ultraviolet radiation absorbing agent is 2-ethylhexyl-p-dimethyl aminobenzoate, 2-hydroxy-4-methoxy benzophenone, or para-aminobenzoic acid.

9. The composition according to claim 7 wherein the amount of urea is from about 0.1 to about 40 percent, and the ultraviolet radiation absorbing agent is from about 1 to about 10 percent, based on the weight of the composition.

10. The composition according to claim 7 wherein the amount of urea is from about 1 to about 20 percent.

11. The composition according to claim 8 wherein the amount of ultraviolet absorbing agent is from about 1-10 percent based on the weight of the composition.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US85/01066

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) 3

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. Cl. (4) A61K 7/42; A61K 7/44

U.S. Cl 424/59; 424/60

II. FIELDS SEARCHED

Minimum Documentation Searched 4	
Classification System	Classification Symbols
U.S.	424/59, 60

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched 5

III. DOCUMENTS CONSIDERED TO BE RELEVANT 14

Category 6	Citation of Document, 16 with indication, where appropriate, of the relevant passages 17	Relevant to Claim No. 18
X	DE,A, 1,767,165, Joos, 09 September, 1971, Example 6	1 to 11
X	DE,A, 2,703,185, Moller et al, 10 August 1978, page 16, lines 27 to 34	1 to 11
X	DE,A, 2,706,782, Kaplan et al, 01 September 1977, page 7, lines 5 to 22	1 to 11
X	N, The Principles and Practice of Modern Cosmetics, issued March, 1963, Vol. 2 R. G. Harry, See pages 520 to 523	1 to 11
X	N, Handbook of Nonprescription Drugs, issued 1977, American Pharmaceutical Association, See pages 280 to 287, 324 to 328 and 336-338	1 to 11

6 Special categories of cited documents: 15

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search 2	Date of Mailing of this International Search Report 2
02 August 1985	14 AUG 1985
International Searching Authority 1	Signature of Authorized Officer 20
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